petition attached 2002 #6

BOX PATENT EXT. DAC

OFFICE OF PETITIONS
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07/715,439

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Atty. Docket No. 080618/0209

In re: U.S. Patent No. 5,153,222

Patentee: Anjaneyulu TADEPALLI, *et al.*

Assignee: United Therapeutics, Corp.

Issue Date: October 6, 1992

REQUEST FOR EXTENSION OF PATENT TERM UNDER 35 U.S.C. § 156

Commissioner of Patents and Trademarks
Washington, D.C. 20231
BOX PATENT EXT.

Sir:

Pursuant to Section 201(a) of the Drug Price Competition and Patent Term Restoration Act of 1984, 35 U.S.C. § 156, United Therapeutics, Corp. ("United Therapeutics"), represents that it is the owner of record of United States Patent No. 5,153,222 (see Exhibit A, assignment record) and hereby requests an extension of the patent term of U.S. Patent No. 5,153,222.

The following information is submitted in accordance with 35 U.S.C. § 156(d) and 37 C.F.R. §1.740, and follows the format and requirements set forth in 37 C.F.R. § 1.740.

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01 FC:111 1120.00 OP

(1) "A complete identification of the approved product as by appropriate chemical and generic name, physical structure or characteristics." 37 C.F.R. §1.74(a)(1)

The approved product is REMODULIN™ (Treprostinil sodium), Injection, 1.0, 2.5, 5.0 and 10.0 mg/ml. The generic name for the approved product is treprostinil, which is indicated for the treatment pulmonary arterial hypertension. Synonyms for Treprostinil sodium are:

UT-15,

LRX-15,

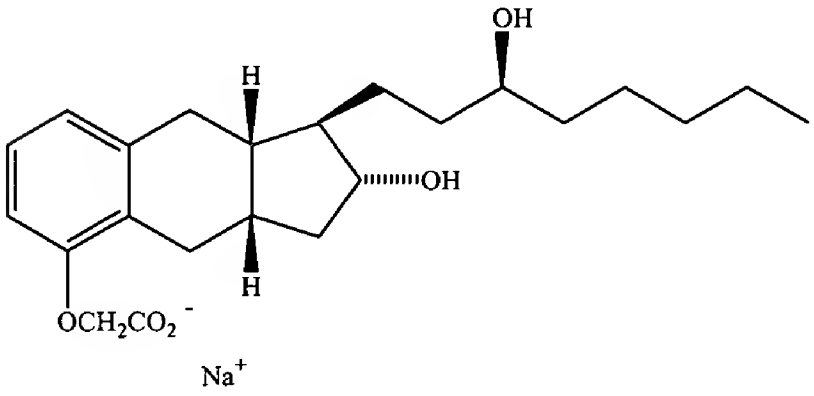
15AU81,

BW A15AU, and

U-62,840.

Treprostinil sodium is identified by the following:

(a) Structural Formula:



(b) Chemical Names:

[[(1*R*,2*R*,3a*S*,9a*S*)-2,3,3a,4,9,9a-hexahydro-2-hydroxy-1-[(3*S*)-3-hydroxyoctyl]-1*H*-benz[*f*]inden-5-yl]oxy]acetic acid and

9-deoxy-2',9$_\alpha$-methano-3-oxa-4,5,6-trinor-3,7-(1',3'-interphenylene)-13,14-dihydro-prostaglandin F_1.

(c) Molecular Weight: 390.52

(d) Empirical Formula: $C_{23}H_{34}O_5$

(2) "A complete identification of the Federal statute including the applicable provision of law under which the regulatory review occurred, " 37 C.F.R. § 1.740(a)(2).

Section 505 of the Federal Food, Drug, and Cosmetic Act (FDC Act), 21 U.S.C. § 355, is the Federal statute under which the Food and Drug Administration's (FDA's) regulatory review of United Therapeutics's REMODULIN™ new drug application (NDA) for Treprostinil sodium occurred. Section 505(b) of the FDC Act, 21 U.S.C. § 355(b), authorizes the filing of an NDA for a "new drug." FDA subsequently approved the REMODULIN™ NDA (NDA 21,272) under the authority granted the agency by Section 505(c) of the FDC Act, 21 U.S.C. & 355 (c).

(3) "An identification of the date on which the product received permission for commercial marketing or use under the provision of law under which the applicable regulatory review period occurred," 37 C.F.R. § 1.740(a)(3).

On May 21, 2002, the FDA approved United Therapeutic's REMODULIN™ (Treprostinil sodium) NDA under section 505 of the FDC Act. Approval of the NDA authorizes the first commercial marketing of Treprostinil sodium.

(4) "In the case of a drug product, an identification of each active ingredient in the product and as to each active ingredient, a statement that it has not been previously approved for commercial marketing or use under the Federal Food, Drug and Cosmetic Act, the Public Health Service Act, or the Virus-Serum-Toxin Act, or a statement of when the active ingredient was approved for commercial marketing or use (either alone or in combination with other active ingredients), the use for which it was approved, and the provision of law under which it was approved," 37 C.F.R. § 1.740(a)(4).

The active ingredient in REMODULIN™ Injection is treprostinil sodium. No product containing treprostinil or treprostinil sodium has been previously approved for marketing under the Food, Drug and Cosmetic Act, the Public Health Service Act or the Virus-Serum-Toxin Act.

(5) "A statement that the application is being submitted within the sixty day period permitted for submission pursuant to § 1.720(f) and an identification of the last day on which the application could be submitted," 37 C.F.R. § 1.740(a)(5)

This application is being submitted within the sixty day period following FDA approval of the REMODULIN™ (treprostinil sodium) NDA. FDA approved the REMODULIN™ (treprostinil sodium) on May 21, 2002. The sixty day period for submission of this patent extension application will expire on July 20, 2002.

(6) "A complete identification of the patent for which an extension is being sought by the name of the inventor, the patent number, the date of issue, and the date of expiration," 37 C.F.R. § 1.740(a)(6).

U.S. Patent No.	5,153,222
Inventor:	Anjaneyulu Tadepelli et al.
Issue Date:	October 6, 1992
Expiration Date:	October 6, 2009

(7) "A copy of the patent for which an extension is being sought including the entire specification (including claims) and drawings," 37 C.F.R. § 1.740(a)(7).

A copy of U.S. Patent 5,153,222 is attached as Exhibit B.

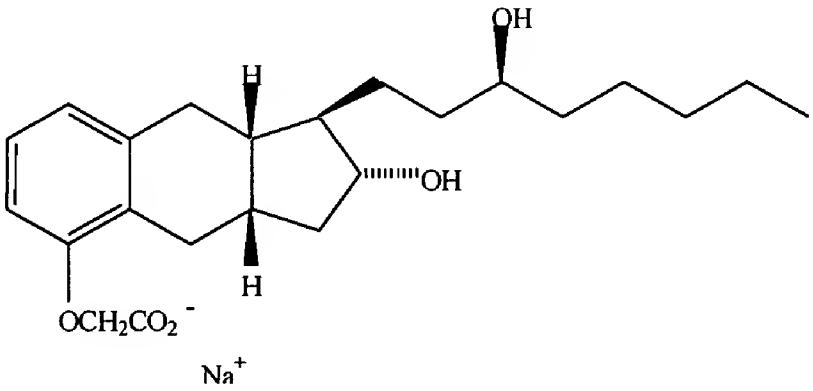
(8) "A copy of any disclaimer, certificate of correction, receipt of maintenance fee payment, or re-examination certificate issued in the patent," 37 C.F.R. § 1.740(a)(8).

U.S. Patent 5,153,222 issued on October 6, 1992 and the first maintenance fee was paid on September 17, 1996. The second maintenance fee was paid on March 29, 2000. A copy of the printout of the Maintenance Status showing the payment is attached as Exhibit C.

No disclaimer, certificate of correction or re-examination certificate has issued in connection with U.S. Patent No. 5,153,222.

(9) "A statement that the patent claims the approved product or a method of using or manufacturing the approved product, and a showing which lists each applicable patent claim and demonstrates the manner in which each applicable patent claim reads on the approved product or method of using or manufacturing the approved product," 37 C.F.R. § 1.740(a)(9).

U.S. Patent No. 5,153,222 claims a method of using the approved product Treprostinil sodium. U.S. Patent No. 5,153,222 claims the approved indication for using Treprostinil sodium. Claims 1 and 2 are directed to the approved method of using REMODULIN for treating an individual with pulmonary hypertension. REMODULIN is an aqueous formulation of a pharmaceutically acceptable salt of [[(1*R*,2*R*,3a*S*,9a*S*)-2,3,3a,4,9,9a-hexahydro-2-hydroxy-1-[(3*S*)-3-hydroxyoctyl]-1*H*-benz[*f*]inden-5-yl]oxy]acetic acid and has the following formula:



Claim 1 and 2 from U.S. Patent 5,153,222 are reproduced below.

1. A method of treating pulmonary hypertension in a patient, which comprises administering to said patient an effective pulmonary hypertension treatment amount of the

compound 9-deoxy-2',9$_\alpha$-methano-3-oxa-4,5,6-trinor-3,7-(1',3'-interphenylene)- 13,14-dihydroprostaglandin F_1.

2. A method of treating pulmonary hypertension in a patient, which comprises administering to said patient an effective pulmonary hypertension treatment amount of a pharmaceutically acceptable salt of the compound 9-deoxy-2',9$_\alpha$-methano-3-oxa-4,5,6-trinor-3,7-(1',3'-interphenylene)- 13,14-dihydroprostaglandin F_1.

35 U.S.C. 156(f) defines "product" to include "any salt or ester of the active ingredient" and section 156(a) indicates that a patent which "claims" a method of using a "product" may be extended. The active ingredient in this case is the compound 9-deoxy-2',9$_\alpha$-methano-3-oxa-4,5,6-trinor-3,7-(1',3'-interphenylene)- 13,14-dihydroprostaglandin F_1, the administration of which to treat pulmonary hypertension is covered in claim 1. The product containing this active ingredient is the sodium salt of that compound, the administration of which to treat pulmonary hypertension is covered in claim 2. Therefore, both claims (claims 1 and 2) are believed eligible for an extension.

The labeling approved by the FDA for treprostinil sodium, which is marketed under the trade name REMODULIN™, states that the drug is "indicated as a continuous subcutaneous infusion for the treatment of pulmonary arterial hypertension in patients with NYHA Class II-IV symptoms to diminish symptoms associated with exercise." The Clinical Pharmacology section of the FDA approved labeling includes a statement that "[t]he major pharmacological actions of treprostinil are direct vasodilation of pulmonary and systemic arterial vascular beds and inhibition of platelet aggregation."

The Drug Interaction section of the FDA approved labeling of Treprostinil sodium (REMODULIN™) includes a statement that "[r]eduction in blood pressure caused by REMODULIN may be exacerbated by drugs that by themselves alter blood pressure, such as diuretics, antihypertensive agents, or vasodilators. Since REMODULIN inhibits platelet aggregation, there is also a potential for increased risk of bleeding, particularly among patients

maintained on anticoagulants. During clinical trials, REMODULIN was used concurrently with anticoagulants, diuretics, cardiac glycosides, calcium channel blockers, analgesics, antipyretics, nonsteroidal antiinflammatories, opioids, corticosteroids and other medications."

(10) "A statement, beginning on a new page, of the relevant dates and information pursuant to 35 U.S.C. § 156(g) in order to enable the Secretary of Health and Human Services . . . to determine the applicable regulatory review period . . . For a patent claiming a human drug . . . the effective date of the investigational new drug (IND) application and the IND number; the date on which a new drug application (NDA) . . . was initially submitted and the NDA . . . number and the date on which the NDA was approved" 37 C.F.R. § 1.740(a)(10)(i).

In order to enable the Secretary to determine the applicable regulatory review period, the following information is provided.

(a) Burroughs Wellcome, filed an Investigational New Drug (IND) application on April 15, 1991, for REMODULIN™ (Treprostinil sodium), which was transferred to LungRx, whose name changed first to LRX Pharmaceuticals and then to United Therapeutics, the current assignee of U.S. Patent No. 5,153,222. The IND was inactivated on April 21, 1994 and reactivated on February 3, 1997.

(b) United Therapeutics initially submitted a new drug application (NDA) for REMODULIN™ (Treprostinil sodium) to the FDA on October 16, 2000, the application was withdrawn on July 5, 2001 and refiled on August 9, 2001.

(c) REMODULIN™ (Treprostinil sodium) was approved by the FDA on May 21, 2002.

(11) "A brief description beginning on a new page of the significant activities undertaken by the marketing applicant during the applicable regulatory review period with respect to the approved product and the significant dates applicable to such activities" 37 C.F.R. § 1.740(a)(11).

Attached is a chronology that briefly describes the significant regulatory activities and relevant dates associated with United Therapeutics's efforts to seek approval of this product before the FDA (Exhibit D).

(12) "A statement beginning on a new page that in the opinion of the applicant the patent is eligible for the extension and a statement as to the length of the extension claimed, including how the length of extension was determined," 37 C.F.R. § 1.740(a)(12).

Statement of Eligibility of the Patent for Extension

(i) It is the opinion of the applicant that U.S. Patent 5,153,222 is eligible for an extension. This opinion is based on the following information on U.S. Patent No. 5,153,222:

(a) 35 U.S.C. § 156(a) - U.S. Patent No. 5,153,222 claims a method of using the approved human drug product REMODULIN™ (Treprostinil sodium).

(b) 35 U.S.C. § 156 (a)(1) - The term of the patent has not expired prior to the submission of this application.

(c) 35 U.S.C. § 156 (a)(2) - The term of said patent has never been previously extended under 35 U.S.C. § 156 (e)(1).

(d) This application for extension is in compliance with 37 C.F.R. § 1.740.

(e) 35 U.S.C. § 156(a)(4) - The product, REMODLUIN™ (Treprostinil sodium), has been subject to a regulatory review period as defined in 35 U.S.C. § 156(g) before its commercial marketing or use.

(f) 35 U.S.C. § 156(a)(5)(A) - The product received permission for commercial marketing or use under the provision of law (i.e., FDC Act § 505) under which the applicable regulatory review occurred.

(g) The application has been submitted within sixty days from the May 21, 2002, approval date.

(h) 35 U.S.C. § 156(c)(4) - No other patent term has been extended for the same regulatory review period for this product.

Statement as to Length of Extension Claimed

The term of U.S. Patent No. 5,153,222 should be extended by 4 years and 333 days, or until September 5, 2014. This term of extension was determined on the following bases.

First, the following calculation of the regulatory review period is in accordance with 35 U.S.C. § 156 and 37 C.F.R. § 1.775. The length of this extension was determined as follows:

(A) The effective date of the Investigational New Drug (IND) application is May 15, 1991, which was thirty days after FDA receipt of the IND on April 15, 1991. The IND number is 36,704.

(B) The new drug application (NDA) for REMODULIN™ (NDA 21-272) was initially submitted to the FDA on October 16, 2000 and received by the FDA on October 16, 2000.

(C) The NDA was approved by the FDA on May 21, 2002.

(D) U.S. Patent No. 5,153,222 was issued on October 6, 1992, and is entitled to a patent term of 17 years from its issue date.

As set forth in 35 U.S.C. § 156(g)(1)(B), the regulatory review period equals the sum of the following periods (i) and (ii):

> (i) the length of time between the date an exemption under §505(i) of the FFDCA became effective (the effective date of the IND) and the date an application was initially submitted under §505 of the FFDCA (the date of the initial submission of the NDA).

An IND for the product was effective on May 15, 1991. The NDA for the product was submitted on October 16, 2000. Thus, for the purpose of this calculation, item (i) for the product equals the number of days from May 15, 1991, to October 16, 2000, or 3471 days.

> (ii) the length of time between the date an application was initially submitted under §505(b) of the FFDCA (the date of the initial submission of the NDA) and the date the application was approved (the approval date of the NDA).

The NDA for the product was submitted on October 16, 2000. The NDA was approved on May 21, 2002. Thus, for the purpose of this calculation, item (ii) equals the number of days from October 1, 1997, to May 21, 2002, or 583 days.

In accordance with 35 U.S.C. § 156(c) and 37 C.F.R. § 1.775, the term of a patent eligible for extension shall be extended by the time equal to the regulatory review period for the approved product which occurred after the date the patent issued. U.S. Patent No. 5,153,222 issued on October 6, 1992. Regulatory review from May 16, 1991-October 6, 1992 is subtracted from the number of days determined to be in the regulatory review period according to 37 C.F.R. § 1.775(d)(1)(i). Thus, for purposes of this calculation, the number of days equals 525 days.

Second, 35 U.S.C. § 156(c) also sets forth the following exceptions (1) - (3) which may operate to shorten the length of the review period used to calculate patent term extension.

> (1) Each period is reduced by any period during which the applicant did not act with due diligence.

There has been no lack of due diligence during the period of regulatory review. Accordingly, no reduction in the review period is required by this provision.

(2) Each period includes only one-half of the number of days in phase (i).

One-half of the number of days in phase (i) equals one-half of 3471 days, or 1736 (calculated 1735.5) days. Adding this number of days to the number of days in phase (ii) (583 days) results in a review period of 2319 days.

The number of days in the review period which were on and before the date on which the patent issued is equal to 525 days. Subtracting this number from the number of days calculated in 35 U.S.C. § 156(c)(2) results in a period of 1794 days (4 years and 333 days) as the period for patent term extension.

> (3) If the period remaining in the patent term after the date of approval of the approved product when added to the regulatory review period as revised under paragraphs (1) and (2) above exceeds fourteen years, the period of extension shall be reduced so that the sum of both periods does not exceed fourteen years.

On the date of approval of the product, May 21, 2002, 7 years and 139 days remained in the term of U.S. Patent No. 5,153,222. Adding this period to the review period calculated above does not yield a period of more than fourteen years.

Third, 35 U.S.C. § 156(g)(6) limits the period of patent term extension to a maximum of five years from the original expiration date of the patent. The original expiration date of U.S. Patent No. 5,153,222 is October 6, 2009. Accordingly, the maximum extension allowed by this provision would extend the term to October 6, 2014. Extension of the patent by the number of days calculated above would not extend the patent beyond October 6, 2014. Accordingly, this provision does not operate to shorten the period of extension to which U.S. Patent No. 5,153,222 is entitled.

Thus, U.S. Patent No. 5,153,222 is entitled to an extension of 4 years and 333 days, to September 5, 2014.

(13) "A statement that applicant acknowledges a duty to disclose to the Commissioner of Patents and Trademarks and the Secretary of Health and Human Services or the Secretary of Agriculture any information which is material to any determination of entitlement to the extension sought," 37 C.F.R. § 1.740(a)(13).

Applicant acknowledges a duty to disclose to the Commissioner of Patents and Trademarks and the Secretary of Health and Human Services or the Secretary of Agriculture any information which is material to any determination of entitlement to the extension sought.

(14) "The prescribed fee for receiving and acting upon the application for extension," 37 C.F.R. § 1.740(a)(14).

Pursuant to 37 C.F.R. § 1.20(j)(1), a check in the amount of $1,120.00 is enclosed with this application.

Should additional fees be necessary in connection with the filing of this paper, or if a petition for extension of time is required for timely acceptance of same, the Commissioner is hereby authorized to charge Deposit Account No. 19-0741 for any such fees. Should a refund of fee paid be necessary, the Commissioner is hereby authorized to credit any such amount to Deposit Account No. 19-0741.

(15) "The name, address and telephone number of the person to whom inquiries and correspondence relating to the application for patent term extension are to be directed," 37 C.F.R. § 1.740(a)(15).

Please direct all inquires and correspondence relating to this application for patent term extension to:

Stephen B Maebius
FOLEY & LARDNER
Washington Harbour, Suite 500
3000 K Street, N. W.
Washington, D. C. 20007-5109
TEL: (202) 672-5569
FAX: (202) 672-5399

(16) "A duplicate of the application papers, certified as such," 37 C.F.R. § 1.740(a)(16).

Enclosed is a certification that this application for patent extension, including its attachments, is being submitted as one original and one duplicate copy thereof (Exhibit E).

(17) "An oath or Declaration as set forth in 37 C.F.R. § 1.740(b)," 37 C.F.R. § 1.740(a)(ii).

The requisite declaration pursuant to 37 C.F.R. § 1.740(b) is attached as Exhibit F.

Respectfully submitted,

July 8, 2002
Date

Stephen B. Maebius
Reg. No. 35,264